REMARKS

Claims 1-58 are pending in the application.

The arguments presented herein raise no new issues, as they relate to an issue of record, the maintained obviousness rejection.

The maintained rejection under 35 U.S.C. § 103 and rejection for obviousness type double patenting are discussed below in the order presented in the final Office Action mailed June 16, 2005.

Rejection under 35 U.S.C. § 103

Claims 1-58 remain rejected as allegedly obvious over Krishna *et al.* (referred to herein as "Krishna") as cited in the previous Office Action. In response to Applicant's arguments filed March 25, 2005, the Examiner contends that one of skill would have been motivated to modify the teachings of Krishna to evaluate primary hydroxylamine compounds because primary N-hydroxylamines would be expected to have the same effects as the nitroxides and corresponding N-hydroxylamines of Krishna on reducing oxidative damage because of structural similarities. The Examiner further argues that one of skill would expect that replacing the alkyl group of a secondary N-hydroxylamine with a hydrogen would lead to a more reactive compound. The Examiner concludes that it would have been obvious to use other N-hydroxylamine compounds and derivatives in view of Krishna because the reaction with the reactive oxygen species is through the hydroxylamine moiety. This rejection is respectfully traversed.

The rejection does not establish a proper case of *prima facie* obviousness

Applicant disagrees for reasons of record. The Examiner has not established a proper case of *prima facie* obviousness. Briefly, Krishna evaluates the effects of changes in the ring structure on antioxidant activity of nitroxides and their corresponding N-hydroxylamines. In order to arrive at Applicant's invention, one of skill would have to replace the very moieties that Krishna was studying with hydrogen. This would have rendered the compounds unsuitable

for Krishna's investigations, as the hydrogen does not form a ring structure (*see, e.g.*, the structures on pages 3479-3483 of Krishna *et al.* and Keana, "*New Aspects of Nitroxide Chemistry*," In *Spin Labeling: Theory and Applications*; cited in Applicant's response filed March 25, 2005). If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion to motivation to make the proposed modification (*see, e.g,* the MPEP § 2143.01). This is the case here. Accordingly, the rejection does not establish a proper case of *prima facie obviousness*.

Pharmaceutical compositions of the invention have unexpected properties

Even assuming *arguendo* that Applicant's invention could be derived from the cited art, the invention is still patentable over this reference. The present claims are drawn to pharmaceutical compositions comprising primary N-hydroxylamines. Applicant has discovered that primary N-hydroxylamines have unexpected properties in comparison to cyclic N-hydroxylamines and their respective nitroxides. The primary N-hydroxylamines of the present invention delay cellular senescence. In contrast, cyclic-N-hydroxlamines (R_2NOH) and their respective nitroxides protect against oxidative damage induced by H_2O_2, but do not delay cellular senescence. This property of primary N-hydroxylamines relative to prior art compounds is taught in the specification, *e.g.*, on page 46, lines 2-7; and page 48, lines 18-24; and page 49, lines 7-11. Applicant additionally teaches that this ability to delay cellular senescence emphasizes the remarkable feature of the primary N-hydroxylamines as antioxidants (page 49, lines 12-13). The presence of a property not possessed by the prior art is evidence of nonobviousness (*see, e.g.*, MPEP § 716.02(a)III). Accordingly, the claimed pharmaceutical compositions comprising primary N-hdyroxylamines are patentable over the cited art.

Obviousness type double-patenting

Claims 1-58 were rejected for alleged obviousness-type double patenting over claims 1-57 of U.S. Patent No. 6,455,589. Applicant submits herewith a terminal disclaimer and a Certificate under 37 C.F.R. § 3.73(b). The terminal disclaimer disclaims the terminal portion

of the term of a patent granted on the instant application over U.S. Patent No. 6,455,589. Applicant notes that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. See, MPEP §804.02.

Claims 1-58 were also rejected for allegedly obviousness type double patenting over claims 1-57 of co-pending application no. 10/713,432. No claims have been allowed in the co-pending application. It is applicant's understanding that if the provisional double patenting rejection is the only rejection remaining in this application, the rejection will be withdrawn in the instant application to permit the application to issue as a patent.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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